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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/851,084	05/09/2001	Normand Brisson	ODDY 001	6912

7590 07/14/2004

EXAMINER
COLLINS, CYNTHIA E

ART UNIT	PAPER NUMBER
1638	

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DATE MAILED: 07/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/851,084	BRISSON ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 May 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 27-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 28-33* is/are rejected.

7)☒ Claim(s) *27* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on May 3, 2004 has been entered.

Claims 7-26 are cancelled.

Claims 1-6 and 27-33 are pending and are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Claim Rejections - 35 USC § 112

Claims 1-6, 28 and 30-33 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the office action mailed September 22, 2003.

Claims 1-6, 28 and 30-33 remain rejected, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of expressing protein fragment complementation assay interacting partners in plant material comprising (A) transforming plant

material with (1) a first construct coding for a first fusion product comprising (a) a first fragment of a dihydrofolate reductase enzyme divided into two fragments whose two fragments can exhibit a detectable enzymatic activity when associated with each other and (b) a first protein-protein interacting domain; and (2) a second construct coding for a second fusion product comprising (a) the second fragment of said enzyme and (b) a second protein-protein interacting domain that can bind (1)(b); culturing said material in the presence of fluorescent substrate and under conditions allowing expression of said PCA interacting partners, and (C) detecting said enzymatic activity by fluorescence microscopy, spectrofluorometry, FACS analysis or a fluorescence-detecting video system, including methods in which the interaction of said protein-protein interaction domains is facilitated by the addition during culturing of an inducer that specifically induces the binding of said protein-protein interaction domains, does not reasonably provide enablement for other methods of expressing protein complementation assay interacting partners in plant material that utilize other types of first molecules. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons of record set forth in the office action mailed September 22, 2003.

Applicant's arguments filed May 3, 2004, have been fully considered but they are not persuasive.

Applicant first points out that "The ability to perform PCA in any cell type, be it bacterial or any eukaryotic cell (including plants) is determined only by whether DNA that encodes for proteins can be introduced into a cell and that under the control of a promoter that can be activated in that cell, the DNA is transcribed into RNA and the RNA translated into protein. This

is true for all of the types of cells that applicants' have discussed in our prior applications, including plant cells, tissues and whole plants as described for the generation of transgenic plants with PCA reporters" (reply page 8).

The rejections are maintained because the specification does not describe or enable a genus of PCA interacting protein partners that interact to reconstitute an enzymatic activity when expressed in plant material. The Examiner disagrees with Applicant's assertion that the ability to perform PCA in any cell type, be it bacterial or any eukaryotic cell (including plants) is determined only by whether DNA that encodes for proteins can be introduced into a cell and that under the control of a promoter that can be activated in that cell, the DNA is transcribed into RNA and the RNA translated into protein. As Applicant notes at page 10 of the reply, the assays will only work if the fused interacting proteins catalyze the reassembly of the enzyme, whose reconstituted enzyme activity must be a measure of the interaction of the fused proteins, which indicates that the ability to perform PCA in a cell such as a plant cell is further determined by the ability of the expressed PCA interacting protein partners being able to interact and being able to reconstitute an enzymatic activity when expressed in a cell.

In this regard the full scope of the claimed invention is not enabled because the specification does not provide sufficient guidance with respect to which PCA interacting protein partners would, when expressed in a plant cell, be able to interact, and would further be able to reconstitute an enzymatic activity, and which would not. Such guidance is necessary because it is unpredictable whether any unspecified PCA interacting protein partners would, when expressed in a plant cell, be able to interact, and would further be able to reconstitute an enzymatic activity, because such activities would be affected by multiple variables, variables which include but are

not limited but are not limited to the particular plant species transformed, the type of tissue in which the PCA interacting protein partners are expressed, the stability of the mRNA transcribed from the recombinant protein coding sequence, the translation efficiency of the mRNA transcribed from the recombinant protein coding sequence, the stability of the expressed PCA interacting protein partners, the availability of enzymatic substrate intracellularly, the availability of essential enzymatic cofactors intracellularly, and the ability of the expressed PCA interacting protein partners to reconstitute the specific enzymatic activity in a nonnative cellular environment. Unspecified PCA interacting protein partners could, for example, fail to interact and reconstitute an enzymatic activity due to cellular degradation of the mRNA and/or the enzyme fragments. Unspecified PCA interacting protein partners could, for example, interact but fail reconstitute an enzymatic activity due to the intracellular presence of an enzymatic substrate or the intracellular absence of essential enzymatic cofactors.

See, for example, Florack et al.(Transgenic Research, 1995, Vol. 4, pages 132-141), who teach that the level of mRNA encoding cecropin B expressed in transgenic tobacco plants varied (0.02% to 0.6% of polyadenylated mRNA) depending on the transformation construct used (page 136 Figure 2), but that cecropin B protein was not detected in any of the plants tested, most likely due to degradation of expressed cecropin B protein (page 136 paragraph spanning columns 1 and 2; page 137 column 1 first paragraph; page 139).

Given the unpredictability of any unspecified PCA interacting protein partners interacting and reconstituting an enzymatic activity when expressed in a plant cell, it would require undue experimentation for one skilled in the art to determine which PCA interacting protein partners to express in a plant cell, as one skilled in the art would have to test by trial and error all available

PCA interacting protein partners for their ability to interact and reconstitute an enzymatic activity when expressed in a plant cell, and/or develop new PCA interacting protein partners that have the ability to interact and reconstitute an enzymatic activity when expressed in a plant cell.

Applicant also points out that it has shown how to select, enable and design a reporter molecule i.e., an enzyme reporter and what are the requirements for successfully performing a PCA using the multitude of reporters which have been exemplified in its prior US patent No. 6,270,964 (reply pages 8-9). Applicant points in particular to column 3, line 58 through column 4, line 42 of its US patent No. 6,270,964 as setting forth the requirements for designing a protein complementation assay (PCA), and further asserts that the criteria do not all need to be satisfied for a proper working of the present invention. Applicant additionally points to Figure 1 of its US patent No. 6,270,964 as showing a general description of a PCA, and further asserts that these assays will only work if the fused interacting proteins catalyze the reassembly of the enzyme, whose reconstituted enzyme activity must be a measure of the interaction of the fused proteins. (reply pages 9-10).

The Examiner reiterates that the status of the instant application as a CIP of US serial number 09/017,412, issued as U.S. Patent No. 6,270,964, does not provide sufficient guidance to enable the full scope of the claims, as U.S. Patent No. 6,270,964 neither claims nor exemplifies nor provides guidance for performing any method of expressing any type of protein fragment complementation assay interacting partners in plant material.

Claims 4 and 5, and claims 6, 29 and 30 dependent thereon, remain rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "said detectable product", for the reasons of record set forth in the office action mailed September 22, 2003.

The rejection is maintained, as Applicant's reply filed May 3, 2004 does not address this rejection.

Claim 5 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "said detection means", for the reasons of record set forth in the office action mailed September 22, 2003.

The rejection is maintained as Applicant's reply filed May 3, 2004 does not address this rejection.

Claim 6 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite in the recitation of "said enzyme reporter molecule", for the reasons of record set forth in the office action mailed September 22, 2003.

The rejection is maintained as Applicant's reply filed May 3, 2004 does not address this rejection.

Allowable Subject Matter

Claim 27 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Remarks

No claim is allowed.

Claim 27 is objected to.

Claims 1-6 and 28-33 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Cynthia Collins  7/11/04